REMARKS

Examiner Small is sincerely thanked for the helpful telephone conference of Monday, February 10, 2003, in which the status of the claims and the requirement for restriction were discussed. As a result of that discussion, the foregoing Supplemental Preliminary Amendment is presented in order to clarify the status of the claims. Claims 1-5 have been canceled, and replaced by claims 31-35, in order to avoid any ambiguity from the previous preliminary amendment. The dependencies of the remaining claims have been adjusted accordingly.

Applicants wish to reaffirm their election of Group II, which contains claims 5 through 8. It is noted that process claims 35 and 7 are not restricted to the production of any particular compound of formula I, but encompass all of the compounds therein. For example, claim 35 recites the coupling of an acidic acid with a perfluoroalkylamine derivative, to produce a compound of claim 31, and is broad enough to read on production of all compounds of claim 31. Any impression that Applicants may have given the Examiner that the process is restricted to any of the particular compounds of former claims 3 and 4 (now claims 33 and 34) is in error, particularly since there is no election of species requirement in the application.

With respect to the restriction requirement, per se, it is again respectfully submitted that all of the claims in the present application should be maintained together for examination. It is noted that Part 2 of Annex B to the PCT rules provides examples concerning unity of invention, and provides the following example as *having* unity of invention:

claim 1: a method of manufacturing chemical substance X

claim 2: substance X.

claim 3: the use of substance X as an insecticide.

It can be seen that the present claims bear the same relationship as this example, and that unity of invention is present between the compounds, their method of making, and the methods of use. Thus, withdrawal of the requirement for restriction, inasmuch as it separates methods of Group II, and uses of Group VI, VIII and IX, from the compounds.

Moreover, it is respectfully submitted that unity of invention, under so called "Markush practice," is present and that the compound claims should not be separated as they have been done in the present situation. The above noted portion of the annex to the MPEP sets forth the

standard to be applied in intermediate/final product claims. The MPEP states that unity of invention shall be considered to be present in the context of intermediate and final products where the following two conditions are fulfilled:

(A) the intermediate and final products have the same essential structural element, in that:

(1) the basic chemical structures of the intermediate and the final products are the same, or

(2) the chemical structures of the two products are technically closely interrelated, the intermediate incorporating an essential structural element into the final product, and

(B) the intermediate and final products are technically interrelated, this meaning that the final product is manufactured directly from the intermediate or is separated from it by a small number of intermediates all containing the same essential structural element.

It is submitted that this is met in the present situation, where, for example, the intermediate claims all the share the common feature of N-protection by an amido group and/or are phthalimides, e.g., in claims 10-17. Thus, at least groups III and IV should be maintained together. Similar considerations apply to the other groups of the restriction requirement.

Finally, it is submitted that various linking claims are present in the application, maintaining various other groups together without restriction. For example, claim 9 recites a compound obtainable by the method according to claim 35, while claim 20 recites an intermediate obtainable by steps a to i of the method of claim 7. Moreover, claim 22 recites a compound synthesized using as intermediates an intermediate of claim 10, an intermediate of claim 14, and an intermediate also of claim 10. It is submitted that these linking claims militate keeping all the groups together without restriction.

In view of the foregoing discussion, withdrawal of the restriction requirement is again respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR § 1.16 and § 1.17 which may be required to facilitate this filing, or credit any overpayment to Deposit Account #13-3402, two copies of this paper are attached for this purpose.

Respectfully submitted,

[signature]

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VERSION WITH MARKINGS TO SHOW CHANGED MADE

IN THE CLAIMS:

Please cancel claims 1-5 without prejudice or disclaimer.

Please amend claims 6, 7, 9, 21, 26, 28-30 as follows:

6. (Amended) A method according to claim ~~5~~ 35, wherein said coupling is a classical peptide coupling using a derivative of 2-(2-nitro-imidazol-1-yl) acetic acid in which the OH group of thecarboxyl function has been replaced by a good leaving group.

7. (Twice Amended) A method for the synthesis of a compound according to claim ~~1~~ 31 or the corresponding non-labeled form thereof, comprising the steps of:

a) adding a THF solution of 2 of Figure 7 to a suspension of PYBOP in THF followed by Et_3N,
b) adding an amine 1 of Figure 7 and Et_3N to the solution obtained in step (a),
c) adding a catalytic amount to the solution obtained in step (b) of pTsOH and refluxing the solution,
d) cooling the solution obtained after step (c) at ambient temperature and adding a sodium bicarbonate solution,
e) extracting the product obtained after step (d) with ethyl acetate and drying and concentrating the product with ethyl acetate,
f) purifying the residue obtained after step (e) by column chromatography on silica gel,
g) removing traces of water by washing the product of step (f) with trifluoroacetic anhydride,
h) reacting said persulphurated derivative obtained from step (g) with a suitable labelled or non-labelled perfluorinating agent and a suitable oxidant resulting in a compound having a high yield of fluor atom incorporation,

i) deprotecting the nitrogen function, resulting in a perfluoroalkyl amine derivative, and

j) coupling the perfluoroalkyl amine derivative obtained in step (i) with an activated form of 2-(2-nitro-imidazol-1-yl) acetic acid, resulting in the [^{18}F]-labelled or non-labelled perfluorinated-nitroaromatic compound

9. (Twice Amended) A [^{18}F]-labeled compound obtainable by a method according to claim ~~5~~ 35.

21. (Twice Amended) Use of compound according to claim ~~+~~ 31 as bioactive compound.

26. (Twice Amended) A method for the detection of tissue hypoxia in a patient comprising:

- introducing an [^{18}F] labeled nitroimidazole compound of claim ~~+~~ 31 into said patient,

- imaging tissue hypoxia in said patient, and

- quantifying tissue hypoxia in said patient.

28. (Twice Amended) A method for the detection of tissue hypoxia in a tissue comprising:

- introducing an [^{18}F] labeled nitroimidazole compound of claim ~~+~~ 31 into a patient,

-removing a tissue sample from said patient, and

-analysing the emission in said tissue sample by autoradiography.

29. (Twice Amended) A method for the detection of an [^{18}F] labeled bioactive compound in a patient comprising:

- introducing an [^{18}F] labeled bioactive compound according to claim ~~+~~ 31 into said patient,

- imaging the presence of said [^{18}F] labeled bioactive compound in said patient, and

-optionally, quantifying the presence of said [^{18}F] labeled bioactive compound in said patient.

30. (Twice Amended) A method for the detection of [^{18}F] labeled bioactive compound in a tissue comprising:

- introducing an [^{18}F] labeled bioactive compound of claim ~~1~~ 31 into a patient,
- taking a tissue sample from said patient, and
- analysing the emission in said tissue sample by autoradiography.